

PUBLICATIONS

PHARMACOLOGICAL EVALUATION OF NOVEL SULFONYLUREA DERIVATIVES

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Sulfonylurea derivatives were initially developed as antibacterial agents; however, their potent hypoglycemic properties were subsequently discovered. Their mechanism of action involves interaction with sulfonylurea receptors (SUR) expressed on pancreatic β -cells, resulting in the inhibition of ATP-sensitive potassium channels and stimulation of insulin secretion. Currently, sulfonylurea-based drugs remain among the widely used therapeutic agents for the management of type 2 diabetes mellitus. *Glimepiride* represents one of the most effective members of this class, exhibiting not only insulin secretagogue activity but also the ability to enhance peripheral insulin sensitivity [1]. Therefore, the development of novel sulfonylurea derivatives with improved hypoglycemic potential remains an important objective in medicinal chemistry.

In the present study, novel mono- and bicyclic sulfonylurea derivatives were synthesized through the nucleophilic addition of isocyanates to the amino group of bicyclic quinazolinone sulfonamide derivatives. The reaction proceeded with high regioselectivity and efficiency, affording the target compounds in high yields.

The hypoglycemic activity of the synthesized compounds was evaluated in screening studies using an experimental hyperglycemia model induced by a single oral administration of glucose (5000 mg/kg). The test compounds were administered orally at doses of 1, 3, and 5 mg/kg. Maninil® (Berlin-Chemie, Germany) at a dose of 3 mg/kg was used as the reference drug.

The obtained results demonstrated that the synthesized compounds exhibited significant hypoglycemic activity following both single and repeated administration. Among the tested derivatives, the bicyclic sulfonylurea compound showed the highest activity, producing a more pronounced hypoglycemic effect compared with the other investigated compounds. These findings highlight the pharmacological potential of the obtained derivative and support its further investigation as a promising candidate for the development of new hypoglycemic agents. Future studies will focus on elucidating its pharmacological properties, mechanism of action, and efficacy under experimental diabetes conditions.

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References:

1. Kumar R., Saha P., Pathak P., Mukherjee R., Kumar A., Kumar R., *Journal of Medical Pharmaceutical and Allied Sciences*. 2020, 9(6), PS.2605-09.